

AMENDMENT UNDER 37 C.F.R. § 1.114(c)  
Application No.: 10/536,504

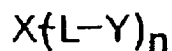
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# AMENDMENTS TO THE CLAIMS

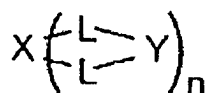
**This listing of claims will replace all prior versions and listings of claims in the application:**

## **LISTING OF CLAIMS:**

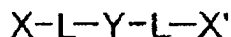
**1. (currently amended):** A prodrug of the general Formula (I), (II) or (III):



( I )



( II )



( III )

in which

X is a tobramycin moiety;

X' is a tobramycin moiety;

L is a linker group ~~is attached to one or more of the hydroxyl or amine groups of the tobramycin moiety, and is~~ for connecting a pharmacokinetic regulator group Y to the tobramycin moiety X or X', the linker group being attached to the tobramycin moiety via any one of the positions 1, 3, 5, 2', 4', 6', 2'', 3'', 4'', or 6'', of the tobramycin moiety, and wherein the linker group includes a functional group capable of being cleaved *in vivo* to expose the tobramycin

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moiety selected from esters, amides, ureas, thioureas, imines, acetals, ethers, phosphates, phosphate esters or diesters, thioesters, oximes and hydrazones;

Y is a pharmacokinetic regulator selected from a hydrophobic moiety or a hydrophilic moiety, wherein the hydrophobic moiety is selected from an optionally substituted straight chain, branched and/or cyclic saturated unsaturated hydrocarbon, and wherein the hydrophilic moiety is selected from oligonucleotides up to 20 nucleotides in length, peptides up to 20 amino acids in length, peptide mimics, carbohydrates, oligosaccharides and derivatives thereof comprising a hydrophobic moiety selected from C<sub>1-20</sub> alkyl, C<sub>2-24</sub> alkenyl, cyclohexyl, aryl or heterocyclyl groups,

the C<sub>1-20</sub> alkyl, C<sub>2-24</sub> alkylenyl groups optionally substituted with a group selected from carboxyl, C<sub>1-6</sub> alkyl, amino and hydroxyl, and optionally interrupted with one or more groups selected from O, C=O, NH, aryl and heterocyclyl,

the aryl and heterocyclyl groups selected from phenyl, biphenyl, pyridyl, indolyl, indolinyl, benzimidazolyl, furanyl, pyrazolyl, isoxazolyl and thiofuranyl, and optionally substituted with a group selected from halo, C<sub>1-4</sub> alkyl, C<sub>1-4</sub> alkoxy, hydroxyl, carboxyl, nitro and OCF<sub>3</sub>;

n is an integer of 1 or greater

or a pharmaceutically acceptable derivative or salt thereof.

**2-6. (canceled).**

**7. (previously presented):** The prodrug according to claim 1, wherein the linker group is selected from the group consisting of an ester, amide, oxime and phosphate.

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**8. (previously presented):** The prodrug according claim 1, wherein the linker group is an ester.

**9. (previously presented):** The prodrug according to claim 1, wherein the pharmacokinetic regulator Y is a hydrophobic moiety selected from an optionally substituted straight chain, branched and/or cyclic saturated or unsaturated hydrocarbon.

**10. (canceled).**

**11. (previously presented):** The prodrug according to claim 9, wherein the hydrophobic moiety is an optionally substituted alkyl or optionally substituted alkenyl having 1 to 24 carbon atoms which is optionally interrupted with oxygen or nitrogen; an optionally substituted aryl; or an optionally substituted heterocyclyl.

**12. (previously presented):** The prodrug according to claim 11, wherein the optionally substituted alkyl or the optionally substituted alkenyl is an optionally substituted C<sub>1-20</sub> alkyl or optionally substituted C<sub>2-20</sub> alkenyl which is optionally interrupted with O, C=O, NH, optionally substituted aryl or optionally substituted heterocyclyl and optionally substituted with carboxyl, optionally substituted C<sub>1-6</sub> alkyl, amino or hydroxyl.

**13. (previously presented):** The prodrug according to claim 11, wherein the optionally substituted aryl is an optionally substituted phenyl or optionally substituted biphenyl.

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**14. (previously presented):** The prodrug according to claim 11, wherein the optionally substituted heterocyclyl is a 5- or 6-membered nitrogen containing heterocyclic group.

**15. (previously presented):** The prodrug according to claim 14, wherein the heterocyclic group is selected from the group consisting of pyridyl, indolyl, indazolyl, 2,3-dihydro-1H-indolyl, furanyl, isoxazolyl, pyrazolyl and thiofuranyl.

**16. (previously presented):** The prodrug according to claim 13, wherein the optional substituents on the phenyl or heterocyclyl are selected from the group consisting of halo, C<sub>1-4</sub> alkyl, C<sub>1-4</sub> alkoxy, hydroxy and OCF<sub>3</sub>.

**17. (previously presented):** The prodrug according to claim 1, wherein the pharmacokinetic regulator Y is a hydrophilic moiety selected from the group consisting of oligonucleotides up to 20 nucleotides in length, peptides up to 20 amino acids in length, peptide mimics, carbohydrates, oligosaccharides and derivatives thereof.

**18. (previously presented):** A method for the preparation of the prodrug of Claim 1 comprising the steps of:

(a) optionally protecting the moieties X and/or X' and/or the linker group which is attached to the optionally protected pharmacokinetic regulator Y;

(b) reacting the optionally protected moieties X and/or X' and the optionally protected linker group L attached to the optionally protected pharmacokinetic regulator Y; and

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(c) if necessary, removing the protecting groups of the moieties X and/or X', the linker L and the pharmacokinetic regulator Y.

**19. (previously presented):** A pharmaceutical formulation comprising the prodrug of claim 1 or a pharmaceutically acceptable salt or derivative thereof, together with one or more pharmaceutically acceptable carriers.

**20. (currently amended):** The pharmaceutical formulation according to claim 19, which further comprises one or more other ~~therapeutic~~ antibacterial ingredients.

**21-22. (canceled)**

**23. (currently amended):** The pharmaceutical formulation according to claim ~~22~~20, wherein the antibacterial agent is effective to treat respiratory infections.

**24. (previously presented):** The pharmaceutical formulation according to claim 22, wherein the antibacterial agent is a combination selected from the group consisting of trimethoprim and sulfonamide; bacitracin and polymyxin B-neomycin; imipenem and fluoroquinolone; and beta-lactam and aminoglycosides.

**25. (previously presented):** An inhaler which comprises a prodrug of claim 1.

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**26. (previously presented):** The inhaler according to claim 25, wherein said inhaler is adapted for oral administration as a free-flow powder.

**27. (previously presented):** The inhaler according to claim 25, wherein said inhaler is a metered dose aerosol inhaler.

**28. (previously presented):** A method for treatment of a bacterial infection comprising the step of administration to a subject in need thereof of an effective amount of the prodrug of claim 1.

**29. (canceled).**

**30. (previously presented):** The method according to claim 28, wherein the infection is a Gram Negative or Gram Positive infection.

**31. (previously presented):** The method according to claim 30, wherein the bacterial infection is associated with the respiratory tract, urinary tract or GI tract or a systemic infection caused by enteric bacteria.

**32. (previously presented):** The method according to claim 28, wherein the administration is to the respiratory tract by inhalation, insufflation or intranasally or a combination thereof.

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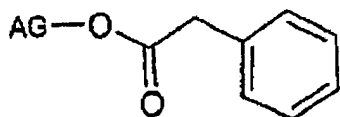
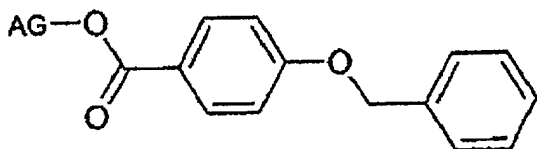
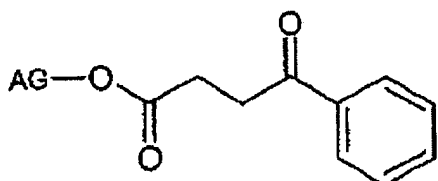
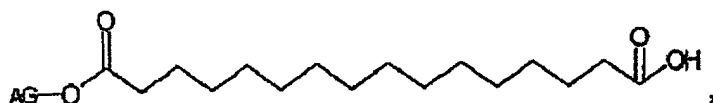
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33-36. (canceled).

37. (previously presented): A method for the detection of a microbial infection which comprises the step of contacting the prodrug of claim 1 with a sample suspected of containing the microorganism.

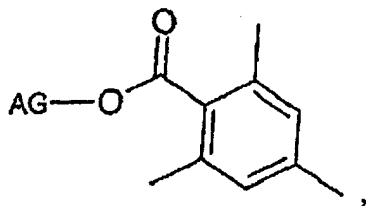
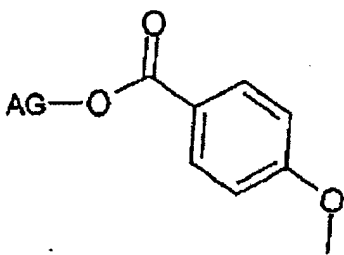
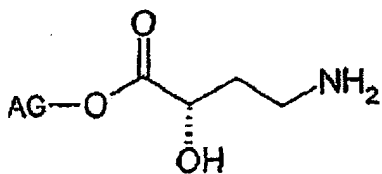
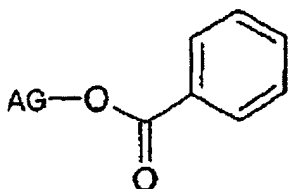
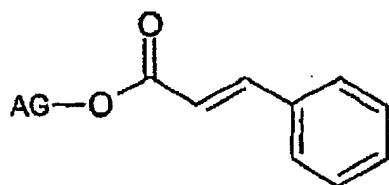
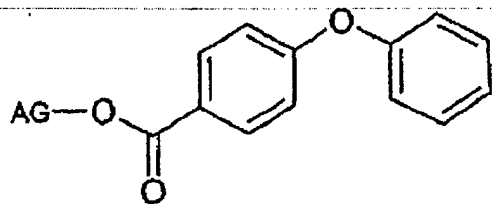
38-105. (canceled).

106. (new): The prodrug according to claim 1, wherein said prodrug is selected from the following



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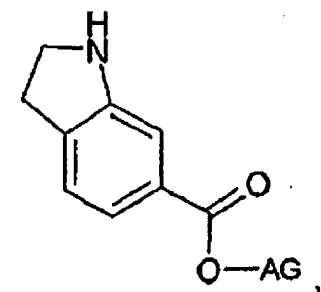
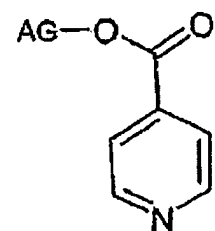
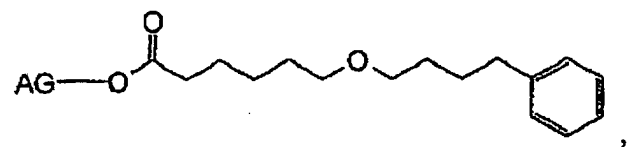
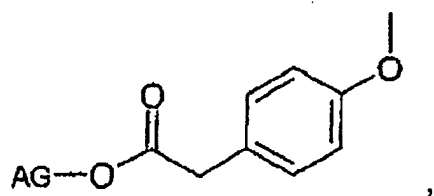
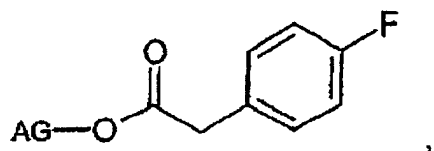
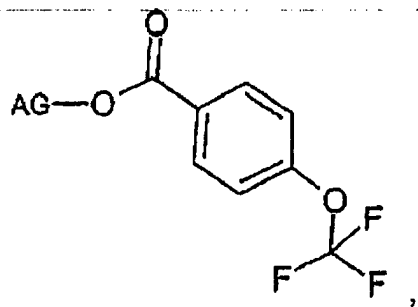
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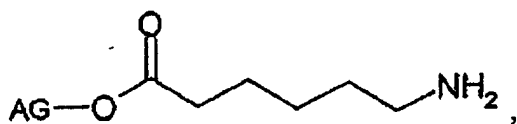
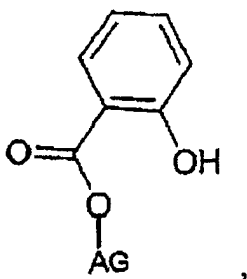
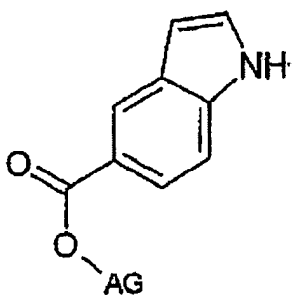
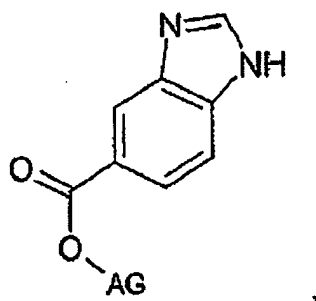
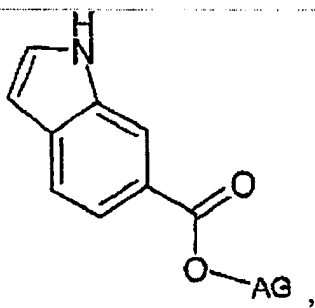
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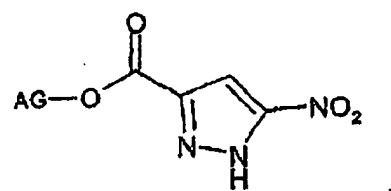
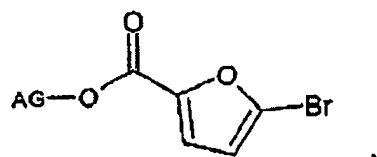
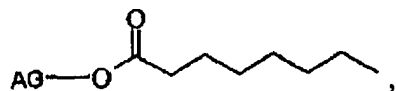
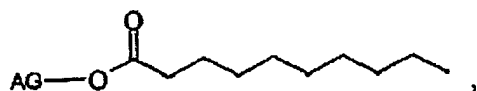
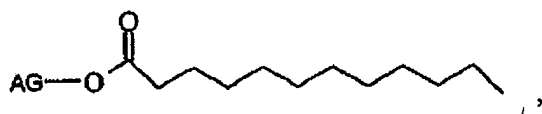
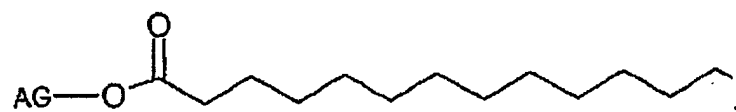
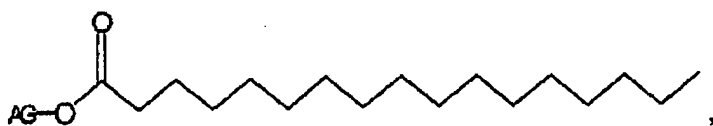
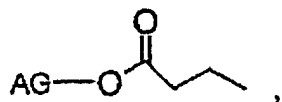
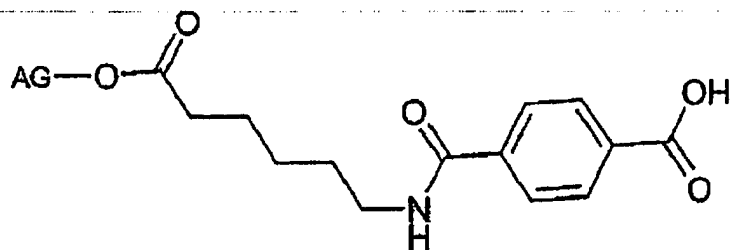
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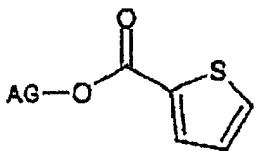
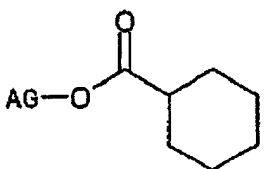
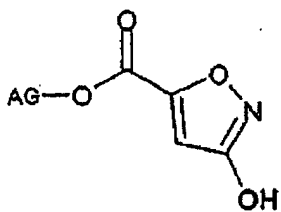
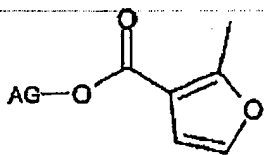
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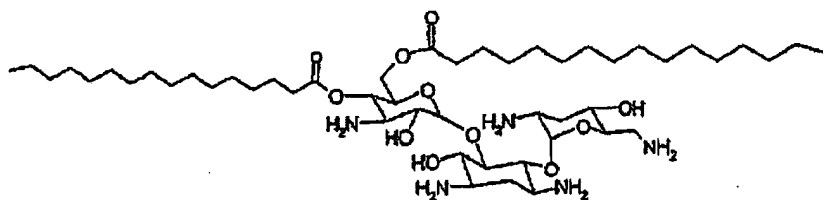
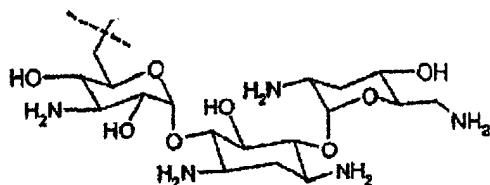


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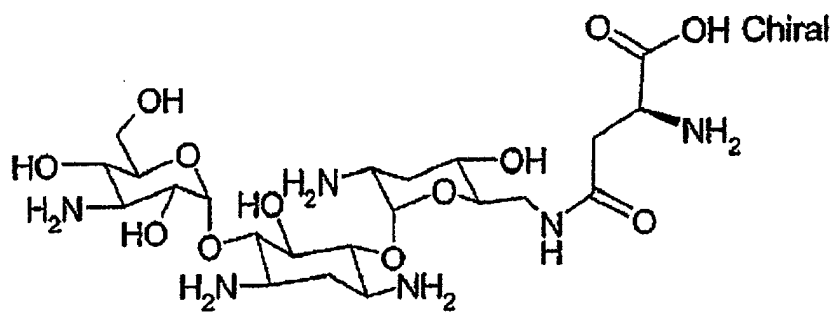
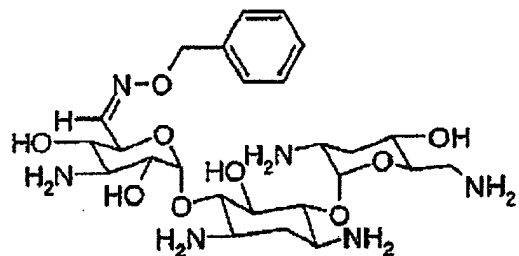
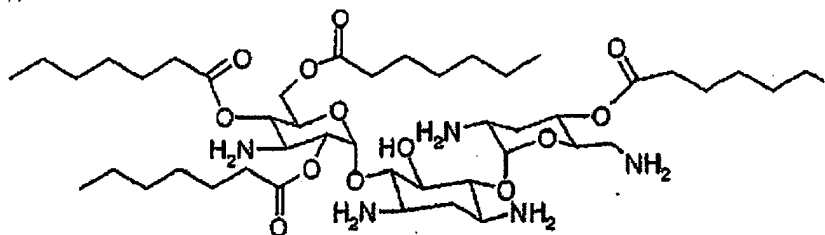
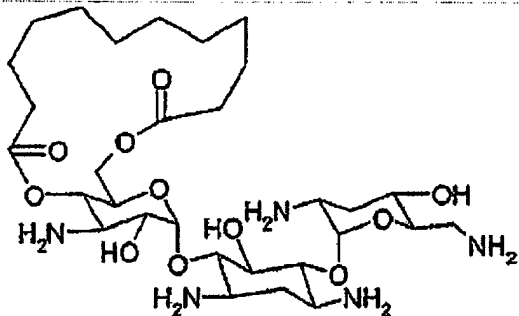


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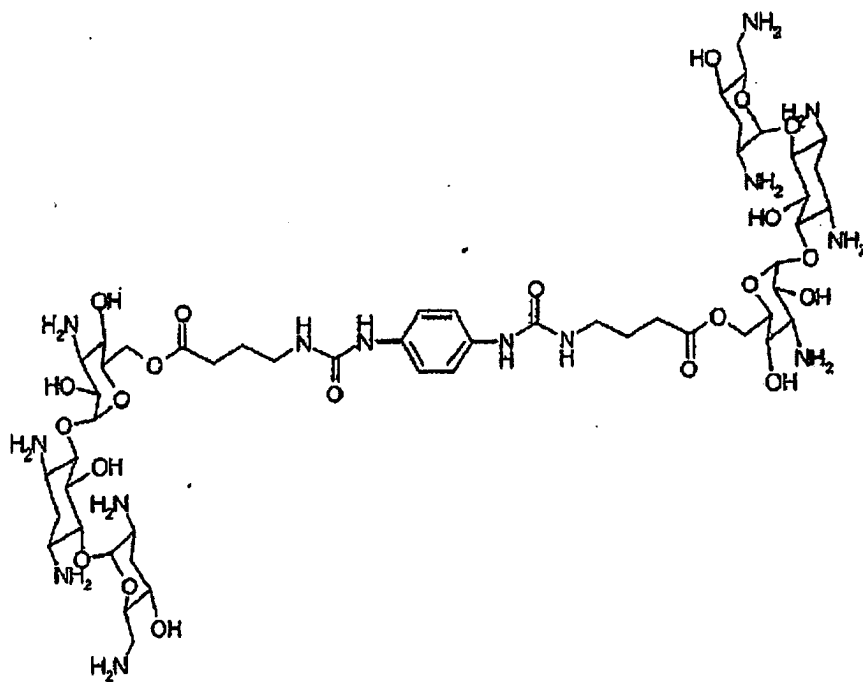
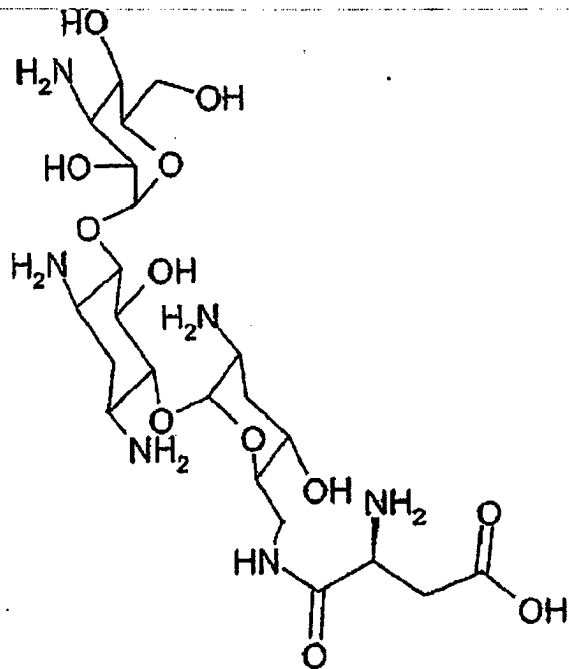
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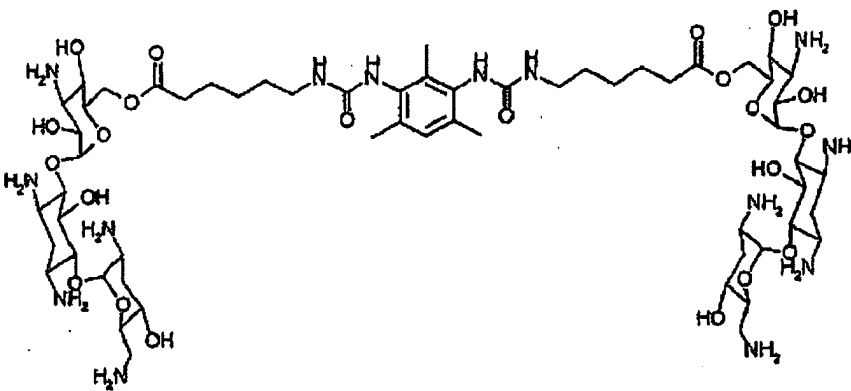
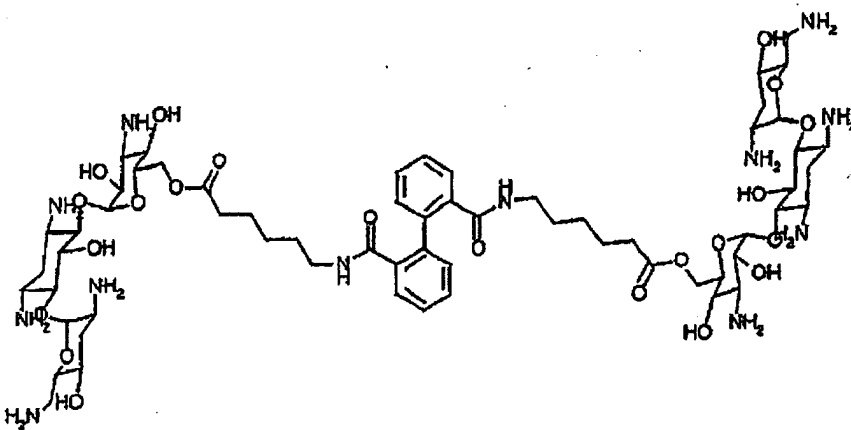
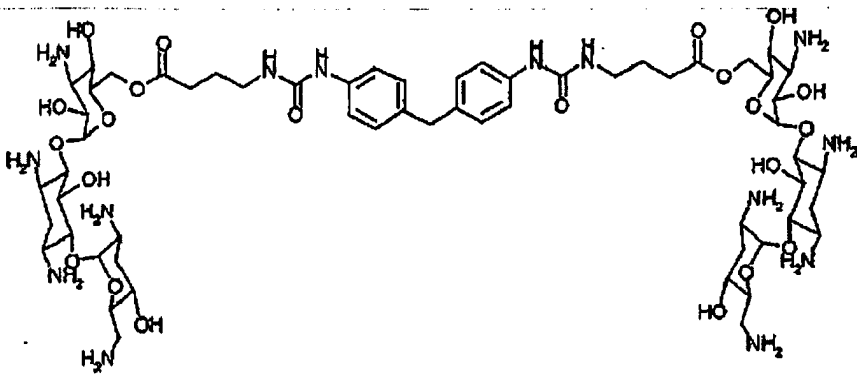
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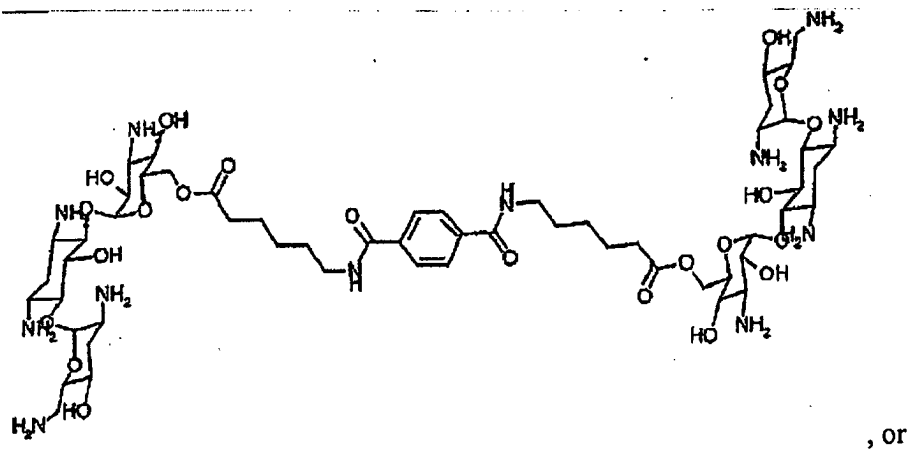
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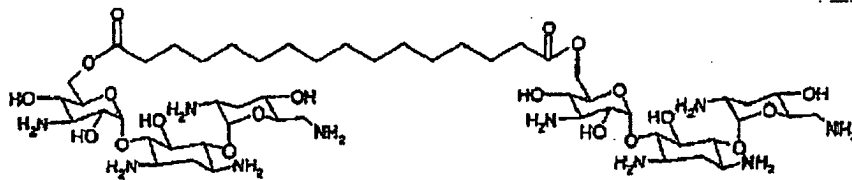


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